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TO: Erin Dunston COMPANY:

Interview Summary	Application No.	Applicant(s)	
	09/656,084	KREISWIRTH ET AL.	
	Examiner	Art Unit	
	Mary K. Zeman	1631	

All participants (applicant, applicant's representative, PTO personnel):

(1) Mary K. Zeman.(3) Stephen Nadich (Appl.)(2) Erin Dunston (Appl Rep).(4) Barry Kreisworth (Appl.)Date of Interview: 01 May 2007.Type: a) ☒ Telephonic b) ☐ Video Conference
c) ☐ Personal [copy given to: 1) ☐ applicant 2) ☐ applicant's representative]Exhibit shown or demonstration conducted: d) ☐ Yes e) ☒ No.

If Yes, brief description: _____

Claim(s) discussed: all pending.Identification of prior art discussed: CDC Plan, VanBelkum, Frothingham.Agreement with respect to the claims f) ☐ was reached. g) ☒ was not reached. h) ☐ N/A.Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: See Continuation Sheet.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN A NON-EXTENDABLE PERIOD OF THE LONGER OF ONE MONTH OR THIRTY DAYS FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WHICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required.

TO: Erin Dunston COMPANY:

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record

A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.132 Interviews Paragraph (b)

In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.

All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:

- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:

- 1) A brief description of the nature of any exhibit shown or any demonstration conducted,
- 2) an identification of the claims discussed,
- 3) an identification of the specific prior art discussed,
- 4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
- 5) a brief identification of the general thrust of the principal arguments presented to the examiner,
(The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
- 6) a general indication of any other pertinent matters discussed, and
- 7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

TO: Erin Dunston COMPANY:

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: The nature of the invention was discussed. Issues regarding the rejection made under 35 USC 112, second paragraph were discussed. Potential amendments to the claims to overcome these rejections were discussed. The rejections under 35 USC 103 over Van Belkum or Frothingham in view of the CDC plan were discussed. The differences between the disclosed method and the methods of the art and state of the art were discussed and clarified. Possible amendments to the claims to obviate these rejections were discussed. The Examiner indicated she would consider entry of an amendment after-final that furthers the prosecution of the application..

Are Variable Repeats in the *spa* Gene Suitable Targets for Epidemiological Studies of Methicillin-Resistant *Staphylococcus aureus* Strains?

In recent communications, Frénay et al. (1, 2) report on molecular typing of methicillin-resistant *Staphylococcus aureus* (MRSA) strains through detailed sequence analysis of the polymorphic repeat region in the staphylococcal protein A encoding *spa* gene. The detection of repeat number variation and numerous sequence variants in the individual repeat units allowed the adequate differentiation of strains from a particular phage type. In conclusion, the authors state that *spa* gene typing may support the hypothesis that MRSA strains of the phage type III-29 belong to a group of closely related clones that have spread throughout Europe individually. Moreover, the authors suggest that *spa* typing may be an important tool in unravelling the spread of MRSA within and between hospitals.

One report by Frénay et al. (1) raises several interesting questions as well as some concerns. As explained below, much relies on the definition of bacterial clonality. Of major importance as well is the epidemiological framework in which the genetic research on MRSA is being carried out. This relates directly to the (working) definition of bacterial clonality and to the extent in which parts of the bacterial genome evolve. The choice of typing procedure, as such, largely determines the outcome of the experiments. This has been demonstrated by comparison of phage typing and genomic screening and comparative analyses of genetic procedures per se for MRSA in particular (3, 4). This is clear from the data described by Frénay et al. (1) as well: a set of strains deemed clonally related by phage typing appears to be more heterogeneous when precise nucleotide data, derived from a single genetic locus, are obtained. Important questions concerning strain relatedness still remain. Which of the two interpretations with respect to genetic (in)equality is correct, or is there no precise answer? Does phage typing underestimate genetic variability, or does protein A gene sequencing lead to an overestimation of phylogenetic distances? Although these questions cannot be answered adequately at present, we have experimental data that may indicate that the latter option is close to the truth. This contrasts with the line of thought as presented by Frénay et al. (1).

We recently analyzed a collection of 121 Danish strains of *Staphylococcus aureus* by phage typing

and random amplification of polymorphic DNA (RAPD) analysis. We detected repeat polymorphisms for both the coagulase and protein A genes (unpublished data). In this collection of strains derived from 20 individuals sampled nasally over time, 24 different genotypes could be defined by RAPD analysis. Interestingly, the major phage type (type 95) coincided with a major genotype, encoded BBB. Surprisingly, this set of strains, apparently clonally related both at the level of phage type and in genomic characteristics as monitored by RAPD, displayed striking heterogeneity in the number of repeats as present in the *spa* gene. Repeat numbers as diverse as 3, 5, 6, 7, 8, 9, to even 10 could be detected. In addition, among the other strains there were several other examples of the same phenomenon. For an extra six genotypes, repeat number variation could be documented. Even without sequence analysis of the individual units, it is obvious that the *spa* repeats may behave in a hypervariable, unstable manner that is unrelated to the overall evolution of the *Staphylococcus aureus* genome. This implies that this marker probably should not be applied for the study of the epidemiological behaviour of this species.

Apparently, the repetitive moiety in the *spa* gene evolves at a speed exceeding that of the overall genome. This implies that clonality among MRSA should not be based on the molecular evolution of the *spa* gene. Hypervariability in other repetitive DNA regions has been demonstrated for a large number of eukaryotes previously (5). Possibly, the *spa* region is a more valuable candidate for tracking sex in populations of gram-positive bacteria.

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References

1. Frénay HME, Bunschoten AE, Schouls LM, van Leeuwen WJ, Vandenbroucke-Grauls CMJE, Verhoef J, Mooi FR: